IN THE CLAIMS

Claim 1 (currently amended) A method of treating female sexual dysfunction comprising administering a therapeutically effective amount of a compound of formula (I), pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof:

$$R^{1}$$
 $CH-CH_{2}$
 $CONH(CH_{2})_{n}-Y$
(I)

wherein

R¹ is C₁₋₆alkyl which may be substituted by one or more substituents, which may be the same or different, selected from the list: halo, hydroxy, C₁₋₆ alkoxy, C₂₋₆ hydroxyalkoxy, C₁₋₆ alkoxy(C₁₋₆alkoxy), C₃₋₇cycloalkyl, C₃₋₇cycloalkenyl, aryl, aryloxy, (C₁₋₄alkoxy)aryloxy, heterocyclyl, heterocyclyloxy, -NR²R³, -NR⁴COR⁵, -NR⁴SO₂R⁵, -COR²R³, -S(O)_pR⁶, -COR⁷ and -CO₂(C₁₋₄alkyl); or R¹ is C₃₋₇cycloalkyl, aryl or heterocyclyl, each of which may be substituted by one or more substituents from said list, which substituents may be the same or different, which list further includes C₁₋₆alkyl; or R¹ is C₁₋₆ alkoxy, -NR²R³ or -NR⁴SO₂R⁵;

wherein

 R^2 and R^3 are each independently H, C_{1-4} alkyl, C_{3-7} cycloalkyl (optionally substituted by hydroxy or C_{1-4} alkoxy), aryl, (C_{1-4} alkyl)aryl, C_{1-6} alkoxyaryl or heterocyclyl; or R^2 and R^3 together with the nitrogen to which they are attached form a pyrrolidinyl, piperidino, morpholino, piperazinyl or N-(C_{1-4} alkyl)piperazinyl group;

 R^4 is H or C_{1-4} alkyl;

 R^5 is C_{1-4} alkyl, CF_3 , aryl, $(C_{1-4}$ alkyl)aryl, $(C_{1-4}$ alkoxy)aryl, heterocyclyl, C_{1-4} alkoxy or -NR 2 R 3 wherein R 2 and R 3 are as previously defined;

 ${\rm R}^6$ is ${\rm C}_{1\text{--}4}$ alkyl, aryl, heterocyclyl or NR $^2{\rm R}^3$ wherein ${\rm R}^2$ and ${\rm R}^3$ are as previously defined; and

 R^7 is C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl or heterocyclyl; p is 0, 1, 2 or 3; n is 0, 1 or 2;

the -(CH $_2$) $_n$ - linkage is optionally substituted by C $_{1-4}$ alkyl, C $_{1-4}$ alkyl substituted with one or more fluoro groups or phenyl, C $_{1-4}$ alkoxy, hydroxy, hydroxy(C $_{1-3}$ alkyl), C $_{3-7}$ cycloalkyl, aryl or heterocyclyl; Y is the group

wherein A is -(CH₂)_q--where q is 1, 2, 3 or 4 to complete a 3 to 7 membered carbocyclic ring which may be saturated or unsaturated; R⁸ is H, C₁-6alkyl, -CH₂OH, phenyl, phenyl(C₁-4alkyl) or CONR¹¹R¹²; R⁹ and R¹⁰ are each independently H, -CH₂OH, -C(O)NR¹¹R¹², C₁-6alkyl, phenyl (optionally substituted by C₁-4alkyl, halo or C₁-4alkoxy or phenyl(C₁-4alkyl) wherein the phenyl group is optionally substituted by C₁-4alkyl, halo or C₁-4alkoxy, or R⁹ and R¹⁰ together form a dioxolane; R¹¹ and R¹² which may be the same or different are H, C₁-4alkyl, R¹³ or S(O)_FR¹³, where r is 0, 1 or 2 and R¹³ is phenyl optionally substituted by C₁-4alkyl or phenylC₁-4alkyl wherein the phenyl is optionally substituted by C₁-4alkyl; or

Y is the group, -C(O) NR¹¹-R¹² wherein R¹¹ and R¹² are as previously defined except that R¹¹ and R¹² are not both H; or Y is the group,

wherein R¹⁴ is H, CH₂OH, or C(O)NR¹¹R¹² wherein R¹¹ and R¹² are as previously defined; when present R¹⁵, which may be the same or different to any other R¹⁵, is OH, C₁₋₄alkyl, C₁₋₄alkoxy, halo or CF₃; t is 0, 1, 2, 3 or 4; and R¹⁶ and R¹⁷ are independently H or C₁₋₄ alkyl; or

Y is the group

wherein one or two of B, D, E or F is a nitrogen, the others being carbon; and R^{14} to R^{17} and t are as previously defined; or

Y is an optionally substituted 5-7 membered heterocyclic ring, which may be saturated, unsaturated or aromatic and contains a nitrogen, oxygen or sulphur and optionally one, two or three further nitrogen atoms in the ring and which may be optionally benzofused and optionally substituted by:

 C_{1-6} alkoxy; hydroxy; oxo; amino; mono or di-(C_{1-4} alkyl)amino; C_{1-4} alkanoylamino; or

 C_{1-6} alkyl which may be substituted by one or more substituents, which may be the same or different, selected from the list: C_{1-6} alkoxy, C_{1-6} alkoxy, C_{1-6} alkylthio, halogen, C_{3-7} cycloalkyl, heterocyclyl or phenyl; or

C₃₋₇cycloalkyl, aryl or heterocyclyl, each of which may be substituted by one or more substituents, which may be the same or different, selected from the list: C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆haloalkoxy, C₁₋₆alkylthio, halogen, C₃₋₇cycloalkyl, heterocyclyl or phenyl;

wherein when there is an oxo substitution on the heterocyclic ring, the ring only contains one or two nitrogen atoms and the oxo substitution is adjacent a nitrogen atom in the ring; or

Y is NR¹⁸S(O)_uR¹⁹, wherein R¹⁸ is H or C₁₋₄alkyl; R¹⁹ is aryl, arylC₁₋₄alkyl or heterocyclyl; and u is 0, 1, 2 or 3.

Claim 2 (currently amended) A compound of formula (I), pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹, n and Y are as defined in claim 1 with the proviso that Y is not the group -C(O)NR¹¹R¹² and when R¹ is propyl or phenylethyl, R¹⁴ is not -CH₂OH.

Claim 3 (currently amended) A compound of formula (I), pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹, n and Y are as defined in claim 1 with the proviso that Y is not the group -C(O)NR¹¹R¹² and R¹⁴ is not H or -CH₂OH.

Claim 4 (original) A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R 1 is C $_{1-6}$ alkyl, C $_{1-6}$ alkoxy, C $_{1-6}$ alkoxy(C $_{1-3}$)alkyl, C $_{1-6}$ alkoxyC $_{1-6}$ alkoxyC $_{1-6}$ alkoxyC $_{1-6}$ alkoxyC $_{1-6}$ alkyl substituted with aryl.

Claim 5 (original) A compound according to claim 4, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹ is C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkoxy(C₁₋₃)alkyl or C₁₋₆alkoxyC₁₋₆alk

Claim 6 (original) A compound according to claim 5, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R^1 is C_{1-4} alkyl or C_{1-6} alkoxy(C_{1-3})alkyl.

Claims 7-13 (withdrawn)

Claim 14 (Original) A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein Y is an optionally substituted 5-7 membered heterocyclic ring.

Claim 15 (original) A compound according to claim 14, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is an optionally substituted aromatic ring.

Claim 16 (original) A compound according to claim 15, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein said aromatic ring is pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, triazolyl, tetrazolyl, oxadiazolyl, thiazolyl, thiadiazolyl, oxazolyl, isoxazolyl, indolyl, isoindolinyl, quinolyl, isoquinolyl, pyridonyl, quinoxalinyl or quinazolinyl each of which may be substituted as defined in claim 1.

Claim 17 (original) A compound according to claim 16, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the aromatic ring is oxadiazole, pyridone or thiadiazole each of which may be substituted as defined in claim 1.

Claim 18 (original) A compound according to claim 17, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the aromatic ring is 1,2,5-oxadiazole, 1,3,4-oxadiazole, 2-pyridone or 1,3,4-thiadiazole each of which may be substituted as defined in claim 1.

Claim 19 (original) A compound according to claim 14, pharmaceutically

acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is substituted by one or more C_{1-6} alkyl, phenyl or phenyl C_{1-4} alkyl.

Claim 20 (original) A compound according to claim 19, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is substituted by C_{1-4} alkyl or benzyl.

Claim 21 (original) A compound according to claim 17, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein when Y is a pyridone said pyridone is *N*-substituted pyridone.

Claims 22-23 (withdrawn)

Claim 24 (original) A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹⁶ and R¹⁷ are hydrogen.

Claim 25 (original) A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein t is 0.

Claim 26 (original) A compound of formula le, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof,

$$HO_2C$$
 $(CH_2)_n$
 $(CH_2)_n$

wherein R¹, Y and n are as defined in claim 2.

- Claim 27 (currently amended) A compound, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, selected from the group consisting of:
- 2-[(1-{[(1-benzyl-6-oxo-1,6-dihydro-3-pyridinyl)amino]carbonyl}cyclopentyl)-methyl]-4-methoxybutanoic acid;
 - 2-{[1-({[3-(2-oxo-1-pyrrolidinyl)propyl]amino}carbonylcyclopentyl]-methyl}-4-phenylbutanoic acid);
 - (+)-2-{[1-({[2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]amino}carbonyl)cyclopentyl]methyl}-4-phenylbutanoic acid;
 - 2-[(1-{[(5-methyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)methyl]4-phenylbutanoic acid;
 - cis-3-(2-methoxyethoxy)-2-[(1-{[(4-{[(phenylsulfonyl)amino]carbonyl}cyclohexyl)amino]carbonyl}cyclopentyl)methyl]propanoic acid;
 - (+)-2-{[1-({[2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]amino}carbonyl)cyclopentyl]-methyl}pentanoic acid;
 - (2R)-2-[(1-{[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)-methyl]pentanoic acid or (-)-2-[(1-{[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)-methyl]pentanoic acid;
 - (2*S*)-2-[(1-{[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)methyl]pentanoic acid or (+)-2-[(1-{[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl}cyclopentyl)-methyl]pentanoic acid;
 - 2-({1-[(3-benzylanilino)carbonyl]cyclopentyl}methyl)pentanoic acid;
 2-[(1-{[(1-benzyl-6-oxo-1,6-dihydro-3-pyridinyl)amino]carbonyl}cyclopentyl)methyl]pentanoic acid;
 - 2-{[1-({[(1R,3S,4R)-4-(aminocarbonyl)-3-butyleyelohexyl]amino}carbonyl)cyclopentyl]methyl}pentanoic acid;
 - trans-3-[1-({[2-(4-chlorophenyl)cyclopropyl]amino}carbonyl)cyclopentyl]-2-(methoxymethyl)propanoic acid;

- trans-3-[1-([[2-(4-methoxyphenyl)cyclopropyl]amino]carbonyl)cyclopentyl]-2-(methoxyethyl)propanoic acid;
- trans-3-[1-({[2-pentylcyclopropyl]amino}carbonyl)cyclopentyl]-2-(methoxyethyl)propanoic acid;
- 3-[1-({[5-benzyl-[1,3,4]-thiadiazol-2-yl]amino}carbonyl)cyclopentyl]-2-(methoxyethyl)propanoic acid;
- 3-[1-({[4-butylpyridin-2-yl]amino}carbonyl)cyclopentyl]-2-(methoxyethyl)propanoic acid;
- 3-[1-({[4-phenylpyridin-2-yl]amino}carbonyl)cyclopentyl]-2-(methoxyethyl)propanoic acid;
- 3-[1-(([1-hydroxymethyl-3-phenylcyclopentyl]amino)carbonyl)cyclopentyl]-2-(methoxyethyl)propanoic acid;
- 2-{[1-({[2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]amino}carbonyl)-cyclopentyl]methyl}-4-methoxybutanoic acid;
- trans-3-[1-({[2-phenylcyclopropyl]amino}carbonyl)cyclopentyl]-2-(methoxyethyl)propanoic acid;
- (R)- 2-{[1-({[2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]amino}carbonyl)-cyclopentyl]methyl}-4-methoxybutanoic acid; and
- $(S)-2-\{[1-(\{[2-(hydroxymethyl)-2,3-dihydro-1\textit{H}-inden-2-yl]amino\}carbonyl)-cyclopentyl]methyl\}-4-methoxybutanoic acid .$

Claim 28 (original) The method according to claim 1 wherein the female sexual dysfunction treated includes at least female sexual arousal dysfunction (FSAD).

Claim 29 (original) The method according to claim 1 wherein the medicament is administered systemically.

Claim 30 (original) The method according to claim 1 wherein the medicament is administered orally.

Claim 31 (currently amended) A method of treatment or prophylaxis of a condition for which a beneficial therapeutic response can be obtained by the inhibition of

neutral endopeptidase comprising administration of a therapeutically effective amount of a compound as defined in claim 2.

Claim 32. (Previously Cancelled)

Claim 33. (Previously Amended) A pharmaceutical formulation comprising a compound as defined in claim 2 together with a pharmaceutically acceptable excipient.

Claim 34. (Previously Amended) A method for the treatment or prophylaxis of female sexual dysfunction comprising administering to the patient a therapeutically effective amount of a compound as defined in claim 2.

Claim 35. (Previously Cancelled)

Claim 36 (currently amended) A process for preparing a compound of formula I or salts thereof

$$HO \longrightarrow \bigcap_{O} \bigcap_{(CH_2)_nY} \bigcap_{(CH_2)_nX} \bigcap_{$$

wherein R¹, n and Y are as defined in any one of claims 2 to 27, comprising the steps of:

a) reacting a compound of formula II

wherein Prot is a suitable protecting group, with a compound of formula Y(CH₂)_nNH₂ (III), to give a compound of formula IV,

Prot
$$O$$
 H $(CH_2)_nY$

then

- b) reacting the compound of formula IV under suitable deprotecting conditions to give the compound of formula I; then
- c) optionally forming a salt.

d)

Claim 37. (original) A compound of formula IV

wherein R¹, n, and Y are as defined in claim 2 and wherein Prot is a protecting group.

drawing (herewith) and amended the specification to include a Brief Description of the Drawings.

The Office Action states that claims 7-13 and 21-23 are withdrawn from further consideration as being drawn to nonelected inventions. The Office Action states that the claims are examined to the extent they read on the elected Y is a HET ring. The Office Action states that Applicants should submit claims limited to the elected invention.

Applicants initially note that claim 21 is directed to a pyridone ring and as such should be included in the elected group. Applicants have herein retained claim 21.

Applicants have noted that claims 7-13 and 22-23 are withdrawn. Claims 32 and 35 were previously cancelled.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter and have not been described in the specification. The rejection states that the claim is addressed to the inhibition of NEP and the treatment of FSD and FSAD. The rejection states that the scope of beneficial in such diverse and subjective areas has not been described. The rejection notes that the term appears to imply the possibility of non-beneficial therapeutic responses.

Applicants traverse the rejection of claims 31 under 35 U.S.C. 112, second paragraph in part based upon their previous response, however, in the interests of expediting prosecution Applicants have herein amended claim 31 by deleting the term "beneficial".

Applicants submit that the amended phrase is fully supported. Applicant further submits that the <u>literal basis</u> for such amendment is not required to be found in the specification (the claim phrase need not be "*in haec verba*" in the specification *In Re Wright* 9 U.S.P.Q.2d 1649, 1651 (Fed. Cir. 1989); Crowne Operations, Int'l, Inc. v. Solutia, Inc. 289 F.3d 1367, 1376 (Fed. Cir. 2002).

Please charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 16-1445. Two copies of this sheet are enclosed.

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Patent Application Attorney Docket No. PC10910ARTB

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